ANNUAL RESEARCH PROGRESS REPORT

(FY 2013)

GRAND FORKS HUMAN NUTRITION RESEARCH CENTER

UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
NORTHERN PLAINS AREA

GRAND FORKS, NORTH DAKOTA 58203

HEALTHY BODY WEIGHT RESEARCH

MANAGEMENT UNIT

5450-010-00

Project Number: 5450-51000-047-00D Accession: 0419639 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: DAVID M KLURFELD Prin Invs: KATE J CLAYCOMBE

Start Date: 05/24/2010 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: BIOLOGY OF OBESITY PREVENTION

Period Covered From: 10 / 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416):

It is not clear whether or how maternal nutrient status during pregnancy epigenetically affects mitochondrial energy metabolism in offspring to increase their susceptibility for developing obesity. Thus, the overall objective is to determine, using animal models, whether low protein intake, high energy intake, or low iron intake during pregnancy influence the development of obesity in offspring through the nutritional programming of mitochondrial function during early development. Specific objectives are: (1) determine whether maternal energy and key nutrient intakes produce epigenetic changes in energy metabolism that contribute to obesity in the offspring, and (2) determine the functional effects of energy, key nutrient intakes and physical activity on obesity-related changes in the expression of genes and protein components of energy metabolism pathways. Within the context of these objectives, the goals of the research are: (1) determine whether protein restriction during pregnancy produces epigenetic changes that, by compromising physiological function, increase the susceptibility of offspring to obesity when fed energy-dense diets; (2) determine whether consumption of diets having excess energy during pregnancy produces long-term mitochondrial dysfunction in offspring that increases their susceptibility to obesity; (3) determine whether low maternal intakes of iron during pregnancy produce mitochondrial dysfunction related to increased susceptibility to obesity in the offspring; and (4) determine whether low maternal intakes of iron during pregnancy impairs mitochondrial adaptation to physical activity in offspring that decreases the effectiveness of physical activity in reducing body weight.

1b. Approach (from AD-416):

Three dietary models will be used with laboratory animals. (1) Female rats will be fed diets containing low or normal levels of protein throughout pregnancy. Immediately after birth, the rats fed low protein diets will be changed to normal protein diets. Half of the offspring born to dams fed low protein diet during pregnancy will be weaned to high fat diets and half will be weaned to normal fat diets. Offspring of dams fed normal protein diet during pregnancy will be treated identically. The offspring will remain on the postweaning diets for the remainder of the experiment. (2) Female rats will be fed high or normal fat diets 14 days prior to conception and throughout pregnancy and lactation. Half of the offspring born to dams fed high fat during pregnancy will be weaned to high fat diets and half will be weaned to normal fat diets. Offspring of dams fed normal fat during pregnancy will be treated identically. (3) Female rats will be fed low or normal iron diets 21 days prior to conception and throughout pregnancy and lactation. Half of the offspring born to dams fed low iron during pregnancy will be weaned to high

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fat diets and half will be weaned to normal fat diets. Offspring of dams fed normal iron during pregnancy will be treated identically. In a variation of the low/normal maternal iron model, the offspring will be maintained on either normal or high fat diets for 8 weeks. At the end of 8 weeks, all the offspring will be given normal fat diet and half will be subjected to exercise for 6 weeks. Offspring will be tested for epigenetic changes, changes in glycolytic and oxidative metabolism, muscle and liver mitochondrial function, and mitochondrial oxidative damage over a period of 6 to 36 weeks after being weaned to their postnatal diets. Epigenetic changes will be assessed by determining DNA methylation and the up- and/or down-regulation of differentially methylated genes will be confirmed by real-time PCR. Measurements of mitochondrial function will include respiration, respiratory complex activity and composition, and reactive oxygen production. Oxidative and glycolytic metabolism will be assessed by measuring the activity of key enzymes in the glycolytic and oxidative pathways. Mitochondria are a major source of reactive oxygen species. Assessment of the outcomes of mitochondrial dysfunction will extend to measurement of oxidative and nitrosative damage to mitochondrial proteins and DNA. For metabolic assessment, blood will be analyzed for glucose, triglyceride, insulin, leptin, and adiponectin concentrations. In addition to body weights, adiposity, lean tissue mass, and total body water components of body composition will be assessed by quantitative magnetic resonance.

2. **Milestones for FY2013:**

1. Protein restriction during pregnancy produces epigenetic changes that, by compromising physiological function, increase the susceptibility of offspring to obesity when fed energy-dense diets.

   36 month milestone: Complete analyses of F1 samples from maternal low protein and postnatal high energy diet studies.
   Milestone Fully Met

2. Complete analyses of F1 samples from maternal high fat and postnatal high energy diet studies
   Milestone Substantially Met

3. Complete analyses for mitochondrial function and biosynthesis in F1 muscle and liver samples and begin analyses for epigenetic changes in F1 samples from maternal low iron studies
   Milestone Not Met
   Other (a reason for not meeting the Milestone other than the ones above)
   The study was not initiated due to retirement of two senior scientists involved in the study
4. Initiate maternal low Fe diet and complete Exercise Component for F1
   Milestone Not Met
   Other (a reason for not meeting the Milestone other than the ones above)
   The study was not initiated due to retirement of two senior scientists involved in the study

3. **Progress Report:**
Objective 1.A. This study determines whether protein restriction during pregnancy produces epigenetic changes that result in obesity in offspring.

The project team conducted studies to determine how prenatal low protein (LP) and postnatal high fat (HF) diets influence obesity, adipose tissue growth, insulin like growth factor 2 (IGF2) gene expression, and energy utilization resulting in obesity and increased risk for type 2 diabetes (T2D) in rats. We demonstrated that prenatal LP and postnatal HF intake increase the rate of adipose tissue growth in offspring through alterations in adipocyte numbers and sizes, expression of the epigenetically imprinted

IGF2 gene, and by affecting adipose tissue energy utilization. Data also demonstrated that these alterations might increase risk for T2D development. This work is in press in Journal of Nutrition.

To determine the mechanisms underlying prenatal low protein (LP) and postnatal high fat (HF) diet-induced obesity and adipose tissue inflammation, we showed that adipose tissue immune cell numbers were increased with HF and decreased with LP diets. In addition to findings from the adipose tissue, data from the liver samples of LP prenatal diet showed decreased expression of genes that are involved in energy production.

Taken together, knowledge gained from our research provides the optimal maternal nutrition information for optimal fetal growth and postnatal development of offspring. We presented these data at the 2013 meeting of the American Nutrition Society; a manuscript is in press in the Journal of Nutrition.

Objective 1.B. This study determines whether consumption of diets having excess energy (high fat or HF) during pregnancy produces long-term mitochondrial dysfunction in offspring that increases their susceptibility to obesity. We have initiated this study and it has a projected completion date of November 2013.

4. Accomplishments

01 Demonstrated that maternal low protein diet followed by a postnatal high fat diet exacerbates obesity and insulin resistance in Sprague Dawley rats. ARS scientists in Grand Forks, ND determined the mechanisms of how maternal undernutrition during pregnancy results in obesity in offspring, especially when challenged postnatally with a high fat diet. When offspring were challenged with the high fat diet after weaning, those who were exposed to maternal low protein diet had greater adipose tissue growth rate, insulin-like growth factor 2 (IGF2) gene expression and IGF2 DNA methylation, and reduced energy utilization in the adipose tissue. Combined with higher serum concentrations of inflammatory cytokines and increased insulin resistance in the same offspring, these findings provided new insight into how low maternal protein intake and postnatal high fat diet contribute to obesity and insulin resistance.

107 3 A 2009

107 4 B 2009

02 Demonstrated that a maternal low protein diet followed by a postnatal high fat diet results in increased adipose tissue inflammation and insulin resistance by increased adipose tissue inflammatory immune cell (macrophage) numbers. ARS researchers in Grand Forks, ND determined the mechanisms underlying prenatal low protein and postnatal high fat diet-induced adipose tissue inflammation. One of the well established characteristics of obesity is accumulation inflammatory immune cells such as macrophages in adipose tissue. Once localized within the adipose tissue from circulating blood, adipose tissue resident macrophages promote adipose tissue inflammation and consequently increased risk for insulin resistance. The research showed that adipose tissue resident macrophage numbers are increased in the high fat fed group regardless of prenatal diet. The data also showed inflammatory subtype macrophage (M2 macrophages) numbers are decreased due to LP prenatal diet. These findings help determine how adipose tissue inflammation caused by inflammatory immune cells contribute to the development of insulin resistance.

107 3 A 2009

107 3 B 2009

03 Demonstrated that a maternal low protein combined with a postnatal high fat diet

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decreased offspring birth weight due to increased energy expenditure in the brown adipose tissue. Offspring of dams fed a low protein prenatal diet have higher resting metabolic rates which are accompanied by greater energy utilization and body temperature. To determine if a prenatal low protein diet increases metabolism, ARS scientists in Grand Forks, ND assessed the expression of genes involved in energy utilization in the brown adipose tissue from the neonates. A maternal low protein diet was associated with reduced birth weights and increased expression of energy utilization genes in the brown adipose tissue. These findings help to understand how prenatal protein restriction increases the risk for low birth weight through increased energy expenditure in the offspring.

107 3 A 2009

107 3 B 2009

04 Demonstrated that maternal low protein and postnatal high fat diets induce obesity by causing epigenetic changes in the offspring's muscle tissues. Muscle tissues are considered metabolically active and utilize stored energy. To determine if maternal low protein intake causes changes in liver and muscle energy utilization and storage in offspring fed high fat postnatal diets, ARS scientists in Grand Forks, ND measured expression of genes that are involved in mitochondrial biogenesis and thermogenesis. The offspring fed low protein prenatal diet had decreased expression of genes located in the liver and muscles that are involved in mitochondrial biogenesis and thermogenesis. Preliminary data indicated that other genes that are regulated epigenetically such as Igf2/H19 locus are differentially methylated due to prenatal low protein and postnatal high fat diets. These findings help to understand how the prenatal maternal diet programs metabolically active tissues in the body to adapt and increase the risk for obesity development when offspring are challenged by high fat diet after weaning.

107 3 A 2009

107 4 B 2009

5. Significant Activities that Support Special Target Populations:

None

6. Technology Transfer:

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
6 Number of Other Technology

Other Technology Details:

01 Description:

Oral presentations at academic institution organized by University of

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North Dakota Biology Department for the Departmental Seminar Series. Title: 'Effects of maternal diet on obesity, adipose tissue energy utilization, and risk for Type 2 diabetes', Sept 2012, Grand Forks, ND.
Transfer: scientific knowledge about maternal diet and epigenetic programming
Customer/user: other scientists/researchers, graduate students, medical students, postdocs, and clinicians
Impact/outcome: sharing of information related to effects of maternal diet on epigenetic changes in adipose tissue leading to obesity and insulin resistance

02 Description:
Poster presentations at international scientific meeting organized by the Obesity Society. Poster title- 'Obesity, adipose tissue mitochondrial function and IGF2 expression are influenced in Sprague Dawley rat offspring by prenatal low protein and postnatal high fat diets", annual Obesity Society meeting, Nov 2013, San Antonio TX.
Transfer: scientific knowledge about brown adipose tissue epigenetic regulation of birth weight and thermogenesis due to pre- and postnatal diets
Customer/user: other scientists/researchers, graduate students, postdocs, clinicians and dietitians
Impact/outcome: sharing of information related to brown adipose tissue energy metabolism and hormonal control of brown adipose tissue thermogenesis

03 Description: Poster presentations at the Epigenetics Symposium organized by University of North Dakota School of Medicine and Heath Sciences. Title: 'Maternal Low Protein Diet Results in Decreased Birth Weight In Male Offspring Due to Increased Energy Expenditure in the Brown Adipose Tissue', Nov 2012, Grand Forks, ND.
Transfer: scientific knowledge about brown adipose tissue metabolism that are affected by maternal diet and resulting in obesity of offspring.
Customer/user: other scientists/researchers, graduate students, postdocs, clinicians and dietitians
Impact/outcome: sharing of information related to brown adipose tissue energy metabolism, and alterations in energy utilization capacity resulting in obesity

04 Description:
Invited oral presentation entitled "Overview of genetics and epigenetics of inflammation: role of nutrition" and participation in focus working group under the topic of 'Inflammation and Nutritional Science for Programs and Policies and Interpretation of Research Evidence (INSPIRE), Organized by the National Institute of Child Health and Human Development, NIH, Bethesda, MD, Nov, 2012.
Transfer: scientific knowledge about Nutrient effects on inflammation, infection, and inflammatory pathway regulated by maternal diets.
Customer/user: other scientists/researchers from NIH, Europe, Universities in US, and USDA
Impact/outcome: Developed a set of guiding principles for the community with regard to how best to deal with the complex interactions between nutrition and inflammation. Two review manuscripts submitted to be

published in Journal of Nutrition, Fall 2013.

05 Description:
Oral presentations at academic institution organized by University of North Dakota School of Medicine and Heath Sciences for The 33rd Annual Frank Low Research Day. Talk title- 'Obesity and Adipose Tissue Epigenetics ', April 2013, Grand Forks, ND.
Transfer: scientific knowledge about maternal diet and epigenetic programming
Customer/user: other scientists/researchers, graduate students, medical students, postdocs, and clinicians
Impact/outcome: sharing of information related to effects of maternal diet on epigenetic changes in adipose tissue leading to obesity and insulin resistance.

06 Description:
Invited oral presentations entitled "Obesity and adipose tissue epigenetics" at the international scientific meeting organized by the American Society for Nutrition, Experimental Biology, April 2013, Boston, MA.
Transfer: scientific knowledge about adipose tissue epigenetic programming that can be affected by maternal and postnatal diet resulting in obesity
Customer/user: other scientists/researchers, graduate students, postdocs, clinicians and dietitians
Impact/outcome: sharing of information related to adipose tissue growth, adipocyte differentiation, cellularity changes due to alterations in energy utilization capacity resulting in obesity

7. International Cooperation / Collaboration

Scientific Publications: Log 115:

1. Zhou, Z., Neupane, M., Zhou, H., Wu, D., Chang, C., Moustaid-Moussa, N., Claycombe, K.J. 2012. Leptin differentially regulates STAT3 activation in the ob/ob mice adipose mesenchymal stem cells. Nutrition and Metabolism. 9:109. 0000277496

Approved: MCGUIRE MICHAEL R Date: 09/30/2013

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ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: JAMES N ROEMMICH

Start Date: 04/21/2011 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416):

Objective 1: Develop and validate assessments of behavioral factors that influence energy intake by a) development and validation of a satiety index of foods that reflects interactions of food with physical activity, body mass index, gender, and age; and b) determination of the effect of exercise on energy intake and eating rate.

Objective 2: Develop methods for assessing patterns of energy expenditure that include a) validation of breath markers as indicators of energy substrate utilization and; b) characterization of seasonal patterns of energy expenditure and balance in free-living individuals using novel applications of existing technologies (e.g., GPS, accelerometry, heart rate monitoring, doubly labeled water).

1b. Approach (from AD-416):

To complete the objectives of this proposal, we will conduct a series of studies with human volunteers. For Objective 1, we will model the satiating effects of selected individual food items and mixed meals. Our model will include the comparisons of hormonal and metabolic responses to food consumption to subjective satiety responses and subsequent energy intake, which we will evaluate in a repeated measures design human trial.
In Objective 2a, we will conduct controlled feeding studies to determine the effects of caloric restriction and exercise on breath markers of substrate utilization. In Objective 2b, we will identify seasonal changes in body fat, as well as where, how much, and when physical activity and dietary intake vary seasonally.

2. Milestones for FY2013:

1. Objective 1 Data analysis and continued experimental human studies.
Milestone Fully Met

2. Objective 2a. Analyze data and continue with experimental human studies; prepare and submit an abstract.
Milestone Fully Met

3. Objective 2b. Enroll 37 subjects. Statistical analysis.
Milestone Fully Met

4. Objective 3a. Develop and refine the protocol and obtain IRB approval; commence

recruitment and initiate experimental human studies.
Milestone Substantially Met

5. Objective 3b. Study putative non-shared experiences associated with energy balance of siblings discordant for adiposity.
Milestone Fully Met

3. Progress Report:
Obj 1a. A pilot study of first 10 participants is complete and data analysis is underway; recruitment of additional participants and additional studies for remainder of project are ongoing.

Obj2a. Data analysis for Expt 2 completed; invention disclosure submitted; abstract and manuscript in preparation. Internal protocol approved for Expt 1; diet designed and analyzed; IRB application approved.

Obj 2b. Data collection for year 1 cohort complete; recruitment for year 2 cohort is complete and data collection underway. Sample and data analysis is in progress and abstracts are in preparation.

Obj 3a. Project developed and reviewed by Center scientists, will be submitted for IRB review.

Obj 3b. Completed follow-up data collection of original cohort of sibling subjects. Developed and received IRB approval for a second cohort of siblings. Data analysis has begun. Began recruitment and study of second cohort.

Ancillary project: examining community-based lifestyle intervention for weight loss and improvements in body composition, fitness, and chronic disease risk biomarkers. All data analyzed; manuscript in review.

Ancillary project: validating use of resonance Raman spectroscopy for measuring skin carotenoids as non-invasive tool to assess fruit & vegetable intake (blood carotenoids are current standard biomarker); in collaboration with investigators at Yale and University of Utah. Data collection complete; analysis nearly complete. Two additional abstracts published (oral and poster). Invited review published; manuscripts in preparation.

Ancillary project: ARS multi-site project "HEALTH" describing barriers and facilitators to following dietary guidelines reported by 5th graders and caregivers. Data collection complete; analysis ongoing. Manuscript in review; two abstracts published (oral and poster), one manuscript published; others in preparation.

Ancillary project: describing barriers and facilitators to following the dietary guidelines reported by 5th grade American Indian children and parents; in collaboration with investigators at Cankdeska Cikina Community College. Data collection complete. Manuscript in review.

Ancillary project: investigating an after-school intervention to increase nutrition knowledge and cooking skills of low-income adolescents and test the use of a mobile phone application for collecting dietary intake data. Data collection complete; analysis nearly complete. One abstract published (oral abstract). Manuscripts in preparation.

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4. Accomplishments

01 Comparison of breath carbon stable isotope ratio before and after exercise can confirm negative energy balance. Demonstrated that comparison of breath carbon stable isotope ratio can be used before and after exercise to determine if a person is in negative energy balance.

107 3 B 2009

02 Skin carotenoids predict plasma carotenoids. Blood levels of carotenoids are considered the best biomarker of consumption of fruit and vegetable (FV) intake by humans. However, blood collection is invasive and not practical for large-scale studies. Skin carotenoid detection based on Raman resonance spectroscopy is a promising new method of non-invasively measuring effectiveness of FV-promoting interventions. ARS scientists at Grand Forks, ND demonstrated that skin carotenoids predict plasma carotenoid levels during a 28-week feeding study with varying levels of vegetables and fruits, confirming that Raman resonance spectroscopy can be reliably used as a non-invasive biomarker of vegetable and fruit intake.

107 2 B 2009

107 3 B 2009

03 Carotenoid-rich diet improves plasma inflammatory markers. Fruits and vegetables contain high levels of carotenoids, compounds that have anti-inflammatory properties. ARS scientists at Grand Forks, ND demonstrated that consumption of a carotenoid-rich diet improves plasma inflammatory markers. Levels of pro-inflammatory cytokines were not changed by depletion of dietary carotenoids, but were decreased upon consumption of a high-carotenoid diet.

107 2 B 2009

04 Subjective assessment of satiety (hunger, fullness) is correlated to plasma ghrelin levels. The subjective assessment of hunger and fullness by responses on a visual analog scale (VAS) were compared to the measured biochemical marker of ghrelin in the blood. The responses of the subjective and biochemical markers to a standard test meal of full fat, sweetened Greek yogurt were highly correlated in each person across three repeated testing periods. These initial results confirm that ARS scientists in Grand Forks, ND have developed a testing method for the satiety value of foods that will allow continued work in this area.

107 2 A 2009

107 3 A 2009

05 Fish for cardiovascular disease risk reduction. ARS scientists in Grand Forks, ND were invited to write a review for a special issue of the journal Nutrients because of their investigations with farmed Atlantic salmon. A paper was written and subsequently published that discusses the role of fish intake on cardiovascular disease reduction in humans. The current intake of fish in the United States and as the fishing industry were discussed. The paper was published in March 2013.

107 2 A 2009

5. Significant Activities that Support Special Target Populations:

None.

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6. Technology Transfer:

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
1 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
24 Number of Other Technology

Invention Disclosure Submitted Details:

01 Docket No: 2112

Title: MATTERN

Descripton: Description: Breath 13C analysis for biofeedback regarding energy balance"
Customer/user: lay people, scientists, health professionals, fitness industry professionals
Impact/outcome: Demonstrated that breath carbon stable isotope ratio can be used to determine an individual's energy balance. This technology could be used by a lay person attempting to lose weight, scientists monitoring compliance to a research diet, or health and fitness professionals needing to know the energy balance of their patients/clients.

Other Technology Details:

01 Description:
Understanding barriers to Dietary Guideline adherence: The HEALTH study (L Jahns). Transfer: oral abstract presentation for International society meeting (October 2012)
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Sharing of GFHNRC research outcomes. Demonstrated that barriers to following the DGA vary by food group.

02 Description:
Nominal group technique elicited barriers and facilitators to following the Dietary Guidelines for solid fats and added sugars in children: The HEALTH study. (L Jahns).
Transfer: poster abstract presentation for International society meeting (October 2012)
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Sharing of GFHNRC research outcomes. Demonstrated that NGT is appropriate for DGA adherence research.

03 Description:
Skin total carotenoids predict plasma carotenoid levels during a 28-week experimental feeding study with varying levels of vegetables and fruit (L Jahns, L Whigham)
Transfer: oral abstract presentation at Experimental Biology meeting.

Boston, MS, April 20-24, 2013.
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Sharing of GFHNRC research outcomes. Demonstrated that skin carotenoids predict plasma carotenoid levels, confirming that Raman resonance spectroscopy can be reliably used as a non-invasive biomarker of vegetable and fruit intake.

04 Description:
Consumption of carotenoid-rich diet improves plasma inflammatory markers. (L Whigham, L Jahns)
Transfer: abstract presentation at Experimental Biology meeting, Boston, MS, April 20-24, 2013.
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Sharing of GFHNRC research outcomes. Demonstrated that consumption of carotenoid-rich diet improves plasma inflammatory markers.

05 Description:
A standardized method of potato preparation and analysis of resistant starch content: Variation by cooking method and service temperature (S Raatz, M Jackson, G Combs)
Transfer: abstract presentation for Experimental Biology meeting (April 2013)
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Sharing of GFHNRC research outcomes. Demonstrated the variability of resistant starch in potato varieties by cooking method and service temperature.

06 Description:
Evaluation of long-chain n3 fatty acid content in diploid and triploid rainbow trout (S Raatz, M Picklo)
Transfer: abstract presentation for Experimental Biology meeting (April 2013)
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Sharing of GFHNRC research outcomes. Demonstrated that farmed triploid trout contain higher levels of omega-3 fatty acids than diploid.

07 Description:
Multiple input modes for context appropriate diet reporting. (L Whigham, J. Roemmich)
Transfer: International Society for Behavior Nutrition and Physical Activity Annual Meeting, Austin, TX, May 23-26, 2012.
Customer/user: scientists, nutritionists
Impact/outcome: Demonstrated that multiple input mode options for a dietary assessment application on a mobile phone device was technically feasible and reduced reporting time.

08 Description:
Dishabituating properties of cognitive and interpersonal stressors. (J.N. Roemmich)
Transfer: The Obesity Society, 30th Annual Scientific Meetings, San Antonio, TX, Sept 20-24, 2012.
Customer/user: scientists, psychologists, nutritionists
Impact/outcome: Demonstrated that psychological stressors dishabituate reductions in responding for food, which may promote greater energy

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intake.

09 Description:
A Built Environment Course Centered on a Quantitative Field Research Experience: Urban Park and College Campus Environments to Promote Physical Activity (J.N. Roemmich)
Transfer: 9th Active Living Research Annual Conference, San Diego, CA, March 12-14, 2012.
Customer/user: scientists, nutritionists, those who design or plan recreational resources for parks or college campuses
Impact/outcome: Demonstrated that women are less physically active than men at both parks and college campuses, and that the built attributes that promote physical activity are very similar across parks and campuses.

10 Description:
Park Visitation, Physical Activity, and Adiposity of Urban Youth (J.N. Roemmich)
Transfer: 10th Active Living Research Annual Conference, San Diego, CA, February, 2013.
Customer/user: scientists, nutritionists, those who design or plan neighborhoods or neighborhood parks
Impact/outcome: Demonstrated that children who visit parks more frequently are more physically active and that park visitation by girls is associated with lower adiposity.

11 Description:
Usability of mobile phone food records to assess dietary intake in adolescents (L. Whigham and J Roemmich)
Transfer: Oral presentation at annual Experimental Biology meeting, Boston, MS, April 20-24, 2013.
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Demonstrated that a food record application on a mobile device could be used to assess dietary intake in adolescents.

12 Description:
Closing the Energy Gap through Passive Energy Expenditure (J Roemmich)
Transfer: Annual Experimental Biology meeting, Boston, MS, April 20-24, 2013
Customer/user: scientists, nutritionists, those who design or plan office environments
Impact/outcome: Demonstrated that standing while performing clerical work expends more energy than while sitting.

13 Description:
Utilization of a dermal carotenoid detection device to quantify changes in fruit and vegetable intake (L Jahns)
Transfer: Invited presentation at Carotenoids Gordon Research Conference, Ventura Beach, CA (January 2013)
Customer/user: scientists
Impact/outcome: Demonstrated that skin carotenoids predict plasma carotenoid levels.

14 Description:
A novel breath biomarker for weight loss (L Whigham)
Transfer: Invited presentation at Augustana College, Sioux Falls, SD (November 2012)

Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Demonstrated that breath stable carbon isotopes can be used as an indicator of energy balance.

15 Description:
Non-invasive assessment of carotenoids as a biomarker of fruit and vegetable intake: The Veg Out Study (L Whigham)
Transfer: Invited presentation at South Dakota State University Nutrition Conference, Brookings, SD (March 2013)
Customer/user: scientists, health professionals, nutritionists
Impact/outcome: Demonstrated that skin carotenoids predict plasma carotenoid levels.

16 Description:
Dietary Fat and Heart Disease (S Raatz)
Transfer: Nutr 8620, Special Topics in Nutrition Science, Department of Food Science and Nutrition, University of Minnesota, 01/ 2, 9, &16/2012
Customer/user: Graduate students in Human Nutrition
Impact/outcome: Taught graduate students principles of research methodology.

17 Description:
Professional Career Options for Registered Dietitians - Clinical Research (S Raatz)
Transfer: FN 340 Seminar in Professional Dietetics, Didactic Program in Dietetics, Southeast Missouri State University, 5/1/2013
Customer/user: Undergraduate students in Dietetics
Impact/outcome: Taught undergraduate students principles of research dietetics.

18 Description:
Enhanced absorption of n-3 fatty acids from emulsified compared with encapsulated fish oil (3/22/13- Keynote address) (S Raatz)
Transfer: 4th Annual Symposium on Functional Foods and Natural Health Products, University of Manitoba, Winnipeg, Manitoba, Canada, 3/22/2013
Customer/user: Graduate students in Human Nutrition and Faculty from across Canada
Impact/outcome: Presented a review of the science of bioavailability of fish oil formulations.

19 Description:
Chronic Stress: No joke for your health (L Jahns)
Transfer: Article in Grand Forks Herald (January 2013)
Customer/user: Public in Greater Grand Forks
Impact/outcome: Nutrition information for the public.

20 Description:
Go Nuts! (S Raatz)
Transfer: Article in Grand Forks Herald (July 2013)
Customer/user: Public in Greater Grand Forks
Impact/outcome: Nutrition information for the public

21 Description:
Satiety & Weight Management (S Raatz)
Transfer: Human Nutritional Sciences Public Lecture, University of Manitoba, Winnipeg, Manitoba, Canada, 3/21/2013
Customer/user: General Public

Impact/outcome: Presented information of the role of satiety in weight management and guidelines for weight reduction diets.

22 Description:
Grand Forks Human Nutrition booth (L Jahns, S Raatz, J Roemmich, L Whigham)
Transfer: Demonstrations at 2013 Health Care Expo, Grand Forks, ND (March 2013)
Customer/user: Public in Grand Forks, ND area; over 2000 attendees
Impact/outcome: Promoted healthy nutrition guidelines for community, enhanced visibility of the GFHNRC, assisted with recruiting volunteers for nutrition studies.

23 Description:
The Crucial Role of Recess (L Whigham)
Transfer: Article in Grand Forks Herald (April 2013)
Customer/user: Public in Greater Grand Forks
Impact/outcome: Educate and motivate the general public about the importance of adequate sleep and the relationship of sleep deprivation to obesity.

24 Description:
Simple Plans to Effectively Achieve Your Health Goals (J Roemmich)
Transfer: Article in Grand Forks Herald (May 2013)
Customer/user: Public in Greater Grand Forks
Impact/outcome: Educate and motivate the general public to use implementation intentions to engage in healthier eating and physical activity habits.

7. International Cooperation / Collaboration

01 UNITED KINGDOM
• Objectives of the research
assessment of genotype as a determinant of carotenoid uptake and conversion efficiency among individuals
• How the work exchange takes place (email, site visits, materials sent, etc.)
Email, materials sent
• Who funds the activity?
ARS and Newcastle University

Scientific Publications: Log 115:

1. Epstein, L.H., Raja, S., Oluyomi, T., Paluch, R.A., Wilfley, D.E., Saelens, B.E., Roemmich, J.N. 2012. The built environment moderates effects of family-based childhood obesity treatment over two years. Annals of Behavioral Medicine. 44:248-258. 0000273950

2. Goldschmidt, A.B., Wilfley, D.E., Paluch, R.A., Roemmich, J.N., Epstein, L.H. 2013. Indicated prevention of adult obesity: reference data for weight normalization in overweight children. Archives of Pediatrics and Adolescent Medicine. 167:21-26. 0000282624

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Project Number: 5450-51000-049-00D Accession: 0421265 FY: 2013

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Approved: MCGUIRE MICHAEL R Date: 09/30/2013

Project Number: 5450-51000-049-03N Accession: 0414947 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: GERALD F COMBS

Start Date: 01/01/2009 Term Date: 12/31/2013

National Programs: 107 N Human Nutrition

Title: GREAT PLAINS HEALTH RESEARCH CONSORTIUM

Period Covered From: 10 / 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-9-0105N

Organization Name: UNIVERSITY NEBRASKA MED CNTR

Progress and Outcomes:

1a. Objectives (from AD-416):

The University of Nebraska Medical Center (UNMC) will bring together regional institutions with a common interest in rural and other health disparities to establish the Great Plains Health Research Consortium (GPHRC). The ARS-Grand Forks Human Nutrition Research Center will be one of the regional research institutions in this consortium.

1b. Approach (from AD-416):

The Great Plains Health Research Consortium will link those research institutions through scientist-to-scientist interactions facilitated by electronic collaboration technologies, and will seek to foster the development of collaborative research projects through the use of funds leveraging, technology/methodology sharing, and some seed funding.

3. Progress Report:

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the UNIVERSITY NEBRASKA MED CNTR. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

This project provided medical oversight of human studies conducted at the GFHNRC. This oversight was provided in the form of direction of the GFHNRC Human Subjects Safety Monitoring Committee which was chaired by a UNMC physician and clinical investigator. The committee oversaw 12 GFHNRC human studies protocols through teleconferences, e-mails and discussions at professional meetings.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, email communications, discussions at professional conferences/meetings, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/20/2013

Project Number: 5450-51000-049-05N Accession: 0419844 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: LISA A JAHNS

Start Date: 07/01/2010 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: GREAT - GRAND FORKS SEASONALITY IN ENERGY BALANCE AND ACTIVE TRANSPORT PILOT STUDY

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-0-0106N

Organization Name: UNIVERSITY OF CALIFORNIA

Progress and Outcomes:

1a. Objectives (from AD-416):

The overall objective of this project is to identify effective ways to facilitate and promote behavior change in individuals and groups to meet dietary and physical activity recommendations for health.

1b. Approach (from AD-416):

We will employ novel field methods and laboratory methods (assessment of energy expenditure by the metabolism of doubly-labeled water, energy substrate assessment by breath carbon isotope ratio, and body composition analysis by DXA) for objective assessment of total energy expenditure, physical activity energy expenditure, and energy intake in free-living individuals. We will link these data to environmental factors (such as season and weather), and to socio-demographic, biological, and psychosocial predictors of energy balance. This study will provide the basis for family-based interventions addressing the identified needs of targeted individuals for maintenance of healthy body weight. The primary outcome measure will be change in weight over time. We propose to build a robust model that can be used to inform family based interventions by including groups of potentially modifying covariates such as age, gender, race/ethnic group, SES, mood, weather, active transport patterns, chronotype, and location. The significance of seasonality will be tested, along with interactions by internal and external factors. Because of the complexity involved in combining data from multiple sources, state-of-the-science tools are needed for data processing, visualization, and analysis. We propose to cooperate with UCSD-EPARC who will provide remote training and support to the GFHNRC team throughout the study period and provide PALMS (Physical Activity Location Measurement System) software.

3. Progress Report:

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the UNIVERSITY OF CALIFORNIA. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

Data collection for year 1 cohort will be completed in late July 2013; recruitment for year 2 cohort is complete and data collection has begun. Sample and data analysis is in progress and abstracts are in preparation.

Project Number: 5450-51000-049-05N Accession: 0419844 FY: 2013

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, email communications, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-049-10S Accession: 0421980 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: GERALD F COMBS

Start Date: 09/01/2011 Term Date: 08/31/2015

National Programs: 107 N Human Nutrition

Title: COMMUNITY NUTRITION AND PHYSICAL ACTIVITY PROGRAM

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-1-0346

Organization Name: GRAND FORKS PARK DISTRICT

Progress and Outcomes:

1a. Objectives (from AD-416):

To evaluate the efficacy and sustainability of diet and physical activity interventions to maintain healthy body weight and reduce risks factors for obesity-related chronic disease in a community setting.

1b. Approach (from AD-416):

The Healthy Body Weight Research Unit will conduct high-impact, community-based research on the roles of diet/physical activity in maintaining healthy body weight. To implement this vision, the Grand Forks Human Nutrition Research Center will collaborate with the Grand Forks Parks District (GFPD, a unit of the North Dakota State government) in conducting human studies designed to support the maintenance of healthy body weight, reduce unhealthy weight gain, and reduce risk of obesity-related conditions. This will involve the use of GFPD facilities, including a community wellness center equipped with a wide variety of exercise equipment (treadmills, step machines, stationary cycles, rowing machines, free weights), indoor pools, indoor/outdoor walking/jogging trails, demonstration kitchen and meeting rooms. These will be used recruit volunteers to studies; conduct diet/physical activity interventions; collect specimens (blood, urine and/or stool samples), and perform a variety of evaluations (anthropometry, body composition, physiological responses to exercise) through study participants. With the results of these studies, the Healthy Body Weight Research Unit will determine the specific features of diet/physical activity practices that contributed to successful healthy body weight management as part of the evidence base for the Dietary Guidelines for Americans process.

3. Progress Report:

This report documents research conducted under a Specific Cooperative Agreement between ARS and the GRAND FORKS PARK DISTRICT. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

Grand Forks Human Nutrition Research Center scientists worked with Grand Forks Park District program planners to complete the monitored physical activity component of a study of the use of parks in Grand Forks, ND, for physical activity of adults and children. This showed that the presence of seats and benches markedly reduced the physical activity of but not the number of people using parks. Planning has been completed for a collaborative study of motivation for physical activity.

Project Number: 5450-51000-049-10S Accession: 0421980 FY: 2013

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, on-site Cooperator/ARS meetings, site visits, email communications, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-049-11S Accession: 0422113 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: LISA A JAHNS

Start Date: 09/15/2011 Term Date: 09/14/2016

National Programs: 107 N Human Nutrition

Title: UTILIZATION OF A SKIN CAROTENOID DETECTION DEVICE TO DETERMINE FRUIT AND VEGETABLE INTAKE

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-1-0355

Organization Name: UNIVERSITY OF UTAH

Progress and Outcomes:

1a. Objectives (from AD-416):

To validate skin carotenoid detection as a marker of fruit and vegetable intake to study the possible health effects that accumulate in human skin, which reflect dietary intake from food sources. Validation through a skin carotenoid detection device would allow researchers better tools for studying strategies to increase fruit and vegetable consumption in large populations and groups of people in whom non-invasive techniques are especially preferred (e.g. children).

1b. Approach (from AD-416):

The Grand Forks Human Nutrition Research Center (GFHNRC) studies healthy diets based on the Dietary Guidelines and how they can help people maintain a healthy body weight, as well as prevent obesity and other chronic health problems. Fruits and vegetables are an important component to a healthy diet and many Americans do not eat the recommended amount of fruits and vegetables. There are many research efforts looking at ways to increase consumption of fruits and vegetables, however, there is a need to develop better ways to assess fruit and vegetable intake in people. Validation of skin carotenoid detection as a marker of fruit and vegetable intake will be accomplished through a controlled feeding study conducted at the GFHNRC. Study volunteers will be fed (on an outpatient basis) a diet initially devoid of carotenoids ("wash-out period") followed by a diet rich in carotenoids. A skin carotenoid detection device will be used to monitor skin carotenoid levels in response to increases in intake of vegetables and fruits.

3. Progress Report:

This report documents research conducted under a Specific Cooperative Agreement between ARS and the UNIVERSITY OF UTAH. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

This research project includes an ancillary project validating the use of resonance Raman spectroscopy for measuring skin carotenoid levels as a non-invasive tool to assess fruit & vegetable (F&V) intake (blood carotenoid levels are the current standard biomarker for F&V intake). This project is a collaboration with investigators at Yale University and the University of Utah. Data collection is complete; data analysis is nearly complete. Two additional abstracts have been published (and presented as an oral and poster abstracts at the annual Experimental Biology meeting). An invited review has

Project Number: 5450-51000-049-11S Accession: 0422113 FY: 2013

been published and manuscripts are in preparation.

Jahns L, Whigham L, Johnson L, Mayne S, Cartmel B, Ermakov I, Gellerman W. Skin total carotenoids predict plasma carotenoid levels during a 28-week experimental feeding study with varying levels of vegetables and fruit. Experimental Biology Meetings, Boston, MA. April 20-24, 2013.

Whigham L, Jahns L, Claycombe K, Johnson L. Consumption of carotenoid-rich diet improves plasma inflammatory markers. Experimental Biology Meetings, Boston, MA. April 20-24, 2013.

Mayne ST, Cartmel B, Scarmo S, Jahns L, Ermakov IV, Gellermann W. Resonance Raman spectrographic evaluation of skin carotenoid status for human studies. Archives of Biochemistry and Biophysics (2013), doi: http://dx.doi.org/10.1016/j.abb.2013.06.007

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, on-site Cooperator/ARS meetings, email communications, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-049-19T Accession: 0421444 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: SUSAN K RAATZ

Start Date: 04/08/2011 Term Date: 05/31/2014

National Programs: 107 N Human Nutrition

Title: GLYCEMIC EFFECT OF HONEY

Period Covered From: 10/ 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-1-0424

Organization Name: NATIONAL HONEY BOARD

Progress and Outcomes:

1a. Objectives (from AD-416):

Honey has been used as a sweetener for centuries. Recent data indicate that honey consumption may have beneficial effects upon glucose intolerance, a health issue currently affecting 57 million Americans of every age and ethnicity. In order to evaluate the glycemic effect of honey, we will carry out a human trial assessing biomarkers of blood glucose responses, insulin sensitivity, and inflammatory markers. Animal studies, using a model of obesity-induced glucose intolerance, will be performed to examine physiologic and biochemical mechanisms by which honey ameliorates obesity-induced glucose intolerance. All studies will be carried out at the USDA Grand Forks Human Nutrition Research Center (GFHNRC).

Our primary objective is to determine the glycemic effects of honey in comparison to sucrose and high fructose corn syrup. We hypothesize that honey will promote improved glucose tolerance and insulin sensitivity compared to both sugar and high fructose corn syrup in normal glycemic and glucose intolerant overweight and obese adults as well as in an animal model of insulin resistance. Our specific aims include (1) evaluation of the effects of the consumption of honey vs. HFCS vs. sugar on glucose tolerance in normoglycemic and glucose intolerant humans, and (2) determine the extent to which honey consumption alters the physiologic and biochemical pathways of glucose intolerance.

1b. Approach (from AD-416):

1) We will evaluate the effect of honey vs. other nutritive sweeteners on insulin sensitivity in 60 overweight adult volunteers. At baseline subjects will be randomized in a Latin square design to one of the nutritive sweeteners (honey, HFCS 55, sucrose) and undergo an oral glucose tolerance test (OGTT). They will then consume 50g of CHO of the assigned treatment daily for a 14 day period followed by a repeat OGTT. A wash out period of 1-2 weeks will be carried out before assignment to the 2nd and 3rd treatments.
2) Rodent studies will be performed to complement the clinical studies described above. We will utilize a controlled model of obesity-induced glucose intolerance to define the positive effects of honey consumption upon insulin-resistance, oxidative stress, and inflammation and define the mechanisms for these positive effects.

Progress Report:
This report documents research conducted under a Trust Fund Cooperative Agreement

Project Number: 5450-51000-049-19T Accession: 0421444 FY: 2013

between ARS and the NATIONAL HONEY BOARD. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

Advertisements were placed in the Dakota Student, UND Newsletter, Grand Forks Herald, and Around the Forks Newsletter. We are trying to place ads in the Grand Forks Air Force Base Newsletter. Flyers were printed and dispersed to retail outlets in the area. We also featured the study at the health fair held at the Alerus Center.

A total of 211 people completed the online application, 112 people signed the consent; 30 did not qualify; 13 withdrew after starting the study; 13 declined participation after screening; 3 did not schedule after signing consent; 5 participants were unable to give blood and withdrew; 40 people completed the study; 8 people are currently in the study.

ARS PI monitoring activities to evaluate research progress included: phone calls/ conference calls, email communications, discussions at professional conferences/ meetings, and review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-049-20T Accession: 0422260 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: SUSAN K RAATZ

Start Date: 10/01/2011 Term Date: 12/31/2014

National Programs: 107 N Human Nutrition

Title: BIOAVAILABILITY STUDY OF FISH OILS: EMULSIFIED VS. CAPSULAR TRIGLYCERIDE

Period Covered From: 10 / 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-2-0401

Organization Name: THE DYSON FOUNDATION

Progress and Outcomes:

1a. Objectives (from AD-416):

The primary objective of this investigation is to determine the relative percentage and rate of incorporation of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and total omega-3 (n-3) fatty acids after ingestion of emulsified flavored triglyceride fish oil supplements (Coromega Squeeze™, Coromega Nectar™, and Barlean Swirl™) versus pure encapsulated triglyceride (Nordic Naturals Omega-3 Softgels™) in defined plasma lipid pools.

The primary endpoints to be evaluated include the fatty acid composition of plasma lipids before and after consumption of a single dose of emulsified triglyceride based fish oils and triglyceride of similar n-3 compositions in capsule form. We will measure changes in plasma total, phospholipid, and chylomicron fatty acids.

1b. Approach (from AD-416):

A randomized and crossover design will be employed to compare absorption kinetics of EPA, DPA and DHA in 10 subjects consuming of Coromega Squeeze™, Coromega Necta™r, Barlean Swirl™ emulsified or the equivalent of the parent oil, Nordic Naturals Omega-3 fish oil™. Study subjects will include healthy adults between the ages of 18 to 60. The supplemental doses will be designed to provide equivalent amounts of EPA, DPA and DHA.
Study subjects will randomly receive fish oil as either the Coromega Squeeze', Coromega Nectar' , Barlean Swirl' (to match EPA), or Nordic Omerga-3 Softgel' supplements after an overnight fast. Whole blood samples will be drawn at baseline, immediately prior to supplementation, and at 2, 4, 8, 24 and 48 hours post supplementation. Food will be restricted during the first 8 hours following the administration of test articles. Following the 8-hour sample, subjects will be allowed to return home and consume a low fat diet devoid of long chain omega 3, i.e., no fish meals or eggs until the 48 hour sample has been drawn. The subjects will again be asked to fast overnight and return to the center for the 24 and 48 hour sampling, respectively. The second arm of the study will be repeated 6 weeks following the initial arm to guarantee adequate washout. Subjects will be asked to consume a low n-3 diet between testing periods and will be provided dietary guidance on foods to avoid. Subjects will be asked to complete a "Tolerance Questionnaire" 4 hours after consumption of the fish oil supplement.

3. Progress Report:

Project Number: 5450-51000-049-20T Accession: 0422260 FY: 2013

This report documents research conducted under a Trust Fund Cooperative Agreement between ARS and the THE DYSON FOUNDATION. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

46 participants applied for online for the study. Of those 19 completed consent and were screened for study participation. - 3 did not show up for 1st visit; 2 did not qualify after screening; 4 declined participation due to schedule conflicts. 10 subjects completed all aspects of the trial. The fatty acid analysis is currently being conducted. When received, data will be analyzed and manuscript(s) prepared for publication.

ARS PI monitoring activities to evaluate research progress included: phone calls/ conference calls, email communications, discussions at professional conferences/ meetings, and review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-049-21T Accession: 0422874 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: SUSAN K RAATZ

Start Date: 03/15/2012 Term Date: 12/31/2013

National Programs: 107 N Human Nutrition

Title: LIFESTYLE MODIFICATION AND POTATO CONSUMPTION

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-2-0409

Organization Name: U.S. POTATO BOARD

Progress and Outcomes:

1a. Objectives (from AD-416):

Potatoes are widely used throughout the world as a staple food. Recently, their role in the diet has been questioned, particularly in relation to glycemia and the risk of developing type 2 diabetes mellitus. We challenge that notion, and propose that consuming potatoes as part of a mixed meal can be a healthy adjunct to lifestyle modification for reducing risk markers of cardiometabolic disease. In order to test this hypothesis, we will carry out a controlled feeding trial with overweight/obese volunteers in which we will compare potatoes containing high or low amounts of resistant starch to other commonly consumed carbohydrate sources in a lifestyle modification program. We will assess the effects of those treatments on biomarkers of cardiometabolic risk: blood glucose responses, insulin sensitivity, lipids and inflammatory markers. These studies will be carried out at the USDA Grand Forks Human Nutrition Research Center (GFHNRC).

1b. Approach (from AD-416):

Our primary objective is to compare the cardiometabolic effects of potato consumption to those of commonly consumed carbohydrate sources on glucose tolerance in overweight and obese, glucose intolerant men and women participating in a lifestyle intervention program. We hypothesize that consumption of potatoes is a healthy adjunct to lifestyle intervention in overweight and obese glucose intolerant adults. Our specific aims include: (1) to evaluate of the effects of the consumption of potatoes (high or low resistant starch) vs. commonly consumed carbohydrate sources on glucose tolerance; and (2) to determine the extent to which potato consumption alters markers of lipid metabolism and inflammation in the context of a lifestyle intervention program.

3. Progress Report:

This report documents research conducted under a Trust Fund Cooperative Agreement between ARS and the U.S. POTATO BOARD. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

Advertisements were placed in the Dakota Student, UND Newsletter, Grand Forks Herald, and Around the Forks Newsletter. We are trying to place ads in the Grand Forks Air Force Base newsletter. Flyers were printed and dispersed to retail outlets in the area. We also featured the study at the health fair held at the Alerus Center. We also explored television and internet advertisements. 65 individuals completed the online

Project Number: 5450-51000-049-21T Accession: 0422874 FY: 2013

application. Of those, 9 subjects completed the study in the first group, 9 subjects are currently in the second group, 2 people didn't show for their information meeting, 14 declined to participate, 4 did not reply, 7 had a BMI > 39.9, 1 had a blood glucose > 125 mg/dl, 3 were disqualified due to medications, 1 person was disqualified due to surgery, 1 person was disqualified due to a medical issue, 2 dropped out after starting the meals, 8 are on the list for the next group and 4 are doing other studies.

ARS PI monitoring activities to evaluate research progress included: phone calls/ conference calls, email communications, discussions at professional conferences/ meetings, and review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

MANAGEMENT UNIT

5450-020-00

Project Number: 5450-51000-045-00D Accession: 0418779 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: DAVID M KLURFELD Prin Invs: HUAWEI ZENG

Start Date: 03/17/2010 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416):

Determine the dietary modulation of obesity-related cancer by selenium. Specific objectives include 1) Characterize interactions of energy imbalance and dietary Se status on obesity-promoted carcinogenesis; 2) Elucidate the relationship of body mass index (BMI) and features of Se metabolism in selenoprotein genotypes differing in cancer risk.

1b. Approach (from AD-416):

This project will determine the extent to which Se counteracts the carcinogenic effects of obesity. It will do so by elucidating the effects of Se status on obesity-promoted mechanisms of carcinogenesis, and the relationships of BMI and Se metabolism among individuals of two genotypes known to differ in cancer risk. Two forms of dietary Se will be used:
i) SeMet, the dominant form of Se in foods;
ii) precursors of CH3SeH - CH3SeCys (catabolyzed to CH3SeH in the cell), the methylseleninic acid (MSeA) (reduced to CH3SeH in the cell), and the combination of SeMet + recombinant methionase (produces CH3SeH).
The project utilizes the complementary expertise of the research team in molecular/cell biology and cell signaling (Zeng), experimental tumorigenesis (Yan, Zeng), human Se metabolism (Combs), and chemistry/ biochemistry (Jackson, Combs). The collaborative nature of the project is evident in the CH3SeH metabolism/action theme that connects the two objectives. This research builds on in-depth expertise and existing collaborations to investigate a highly relevant problem hitherto not addressed. The Grand Forks Human Nutrition Research Center provides this team of investigators with an experienced professional infrastructure for the efficient recruitment and management of human subjects and the controlled use of animal and cell models.

2. Milestones for FY2013:

1. Complete inflammatory cytokine, MAPK/APC pathway and DNA methylation analyses (Subobjective 1A1).
Milestone Fully Met

2. Complete P13K/AKT/mTOR pathway and microRNA analyses (Subobjective 1A2).
Milestone Fully Met

3. Complete data analyses and prepare report for exp 2. Initiate animal feeding, data collection, related assays and analysis for experiments of 2x2x2 factorial

studies on interaction of physical activity, Se and diet-induced obesity on secondary tumor development (Subobjective 1B).
Milestone Fully Met

4. Continue sample collection and analyses (Subobjective 2A).
Milestone Substantially Met

5. Complete sequential flights of Se metabolism studies; publish screening results (Subobjective 2B1).
Milestone Fully Met

6. Validate Se speciation analytical method using animal samples (Exp 2; Hyp 2.B.2) Publish validated method; employ in assessment of human Se status (Subobjective 2B2).
Milestone Substantially Met

3. Progress Report:

1) Although it is known that selenium (Se) may reduce colon cancer risk, the anticancer efficacy of Se against obesity/high-fat diet related colon cancer remains to be elucidated. We hypothesized that CH3SeH, an in vivo Se metabolite pool, reduces the obesity/high fat diet related colon cancer. To determine the extent to which Se reduces obesity/high fat diet related colon cancer, we established an oral daily Se ingestion (in vivo) method in C57/BL mice fed with low/high fat diets. Completed a study on the inhibitory effect of CH3SeH on both colon cancer proliferation (in vitro), tumor growth potential in a colon cancer mouse model (in vivo), and we now are working on molecular/biochemical analysis. In addition, we are establishing chemical (the azoxymethane-AOM) induced colon cancer mouse model which will allow us to study diet and colon cancer risk including both tumor initial and development stages.

2) Butyrate, produced in the colon by the bacterial fermentation of carbohydrate, induces cell growth inhibition in colonic epithelial cells, which may contribute to protection against colon cancer. On the other hand, the cell growth inhibition induced by bile acid deoxycholic acid (DCA) may cause compensatory hyperproliferation of colonic epithelial cells and consequently increase colon cancer risk. We hypothesized that butyrate and DCA may employ different molecular pathways to inhibit cell proliferation. To determine the cellular basis of this opposite effect, we examined the effect of prolonged exposure of butyrate and deoxycholic acid (DCA) on colonic cell proliferation and its related signaling pathways, and found that both butyrate and DCA inhibit colon cell proliferation, each modulates cell cycle and apoptosis via the distinct cellular signaling targets.

3) The roles of selenium in secondary cancer prevention remain largely unexplored. We hypothesized that selenium reduces malignant spread. We completed an animal study that investigated the interaction of selenium and high-fat feeding on secondary tumorigenesis. Furthermore, we complete animal feeding of experiments (1) that assessed the interaction of plasminogen activator inhibitor-1 deficiency and high-fat feeding on malignant spread and (2) that determined the restricted feeding of a high-fat diet on adipogenesis; data generated will be used for designing further studies on selenium and high-fat diet on secondary tumorigenesis.

4) Changes in dietary practice and an increase in physical activity may reduce the risk of obesity. We hypothesized that soy consumption and moderate physical activity reduce the risk of obesity. We completed a 2x2x2 study that assessed interactions of soy protein supplementation and voluntary running on adiposity in high-fat diet-fed mice

and changes in related inflammatory and angiogenic markers and demonstrated both soy protein and voluntary running reduced adiposity and related inflammation and the latter, not the former, was through an action of weight reduction. Our results indicate the usefulness of both soy protein and physical activity in weight management and reducing the risk of obesity.

4. Accomplishments

01 Gut bacteria play a critical role in obesity related fatty liver disease. High-fat diets produce obesity and are linked to the development of nonalcoholic fatty liver disease. ARS researchers in Grand Forks, ND, determined the correlation of fatty liver and predominant gut bacteria in a diet-induced obesity mouse model. These data demonstrated marked changes in increase of gut bacteria with high-fat feeding that were associated with the development of fatty liver. These findings provide new insights into the mechanistic process of diet, obesity and fatty liver.

107 2 A 2009

107 3 A 2009

02 Piperlongumine (PPLGM) compounds activates cell growth related pathway in fighting cancer. PPLGM is a bioactive compound isolated from long peppers that may be used against cancer. To test the hypothesis that PPLGM may work through the cell proliferation pathway, ARS researchers in Grand Forks, ND, identified the contribution of the key cell proliferation pathway in PPLGM-mediated colon cancer cell death. These findings provide new insights into the mechanistic process of PPLGM anticancer property, which is the scientific basis for using PPLGM to prevent colon cancer.

107 2 A 2009

107 3 A 2009

03 Dietary curcumin reduces bone structure. Improvement in survival rate and quality life of cancer patients is the key determining the success of cancer prevention. ARS researchers in Grand Forks, ND, demonstrated that dietary curcumin supplementation reduced bone structure in both non-tumor-bearing and tumor-bearing mice. Curcumin has been investigated as a chemopreventive agent in clinical trials. These results indicate the possibility of combined effect of cancer-induced osteolysis and curcumin-stimulated bone loss in cancer patients using curcumin. Thus, the assessment of bone structure changes should be considered for those patients who participate in curcumin clinical trials to determine its effects on skeletal health.

107 2 A 2009

107 3 A 2009

04 Selenium (Se) transporter, a selenoprotein, is involved in type 2 diabetes / cancer risk, and the data indicate that Se status is related to risk to obesity-related disease. Cellular methylation, a protein medication process, enables expression of glucose formation enzymes and metabolism of the nutrient Se. To test the hypothesis that methylation status may alter the expression of Se-transporter, ARS researchers in Grand Forks, ND, examined/demonstrated that disruption of methylation pathway reduced Se-transporter (SEPP1 protein) expression. This effect is at the level of RNA but not protein. These findings provide the scientific basis of Se intake and potential molecular targets to prevent type 2 diabetes/cancer risk. [Neither dietary selenium nor selenoprotein status affect the incidence of hepatocarcinogenesis driven by TGFa, but their deficiency induces widespread pyogranuloma formation.

107 2 A 2009

107 3 A 2009

05 Demonstrated that genotype influences selenium (Se) metabolism associated with cancer

risk. To test the hypothesis that certain selenoprotein genotypes may affect the rate of Se metabolism, ARS researchers in Grand Forks, ND, examined the extent to which selenoprotein genotypes contribute to interindividual variation in their expression and activity. Our results showed that individuals with certain genotypes at glutathione peroxidase (GPX1) regulate Se metabolism/level which is associated with cancer risk. These studies indicate genetic determinants associated with cancer risk also affect Se status and metabolism - the first evidence of an association of aberrant Se metabolism and cancer risk, providing the metabolic basis for the relationship of obesity and Se metabolism.

107 2 A 2009

107 3 A 2009

06 Demonstrated presence of selenium (Se)-metabolites in animal/human plasma and urine. It has been hypothesized that non-protein fractions such as low molecular weight Se metabolites play a critical role in anticancer action, but to detect/measure these metabolites is a big challenge. ARS researchers in Grand Forks, ND, have optimized the method to eliminate protein-bound Se from samples by organic solvent precipitation and filtration; developed sensitive detection methods for Se-metabolites. These novel analytical methods/ approached will be widely used in future Se research and other related nutritional studies.

107 2 A 2009

107 3 A 2009

5. Significant Activities that Support Special Target Populations:

None

6. Technology Transfer:

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
8 Number of Other Technology

Other Technology Details:

01 Description:

Two presentations at the Federation of American Societies for Experimental Biology. The topics were on the dietary Se intake and colon cancer prevention; gut microbiota and obesity related fatty liver.

Transfer/Customer/user:
New information on Se/colon cancer prevention and gut microbiota/fatty liver was transferred orally to a group of academic and industrial

investigators.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

02 Description:

Presentation "Vitamin D Genetic Variants in Preeclampsia" at 2013 Midwest Nursing Research Society Conference.

Transfer/Customer/user:
New information on the association of vitamin D genetic variants and preeclampsia was transferred orally to a group of academic and healthcare workers.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

03 Description:

Two presentations at 2013 AACR Conference. The topics were on Se intake, exercise and secondary cancer prevention.

Transfer/Customer/user:
New information on Se intake, exercise and secondary cancer prevention was transferred orally to a group of academic and healthcare workers.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

04 Description:

Presentation "Realizing Opportunity" at the opening of the Choice Health and Fitness Center, Grand Forks, ND.

Transfer/Customer/user:
Vision of health practice and research as linked activities to a diversified citizens group.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

05 Description:

Presentation "Opportunities for selenium-enhanced foods in cancer prevention" to annual meeting of the Soil Science Assoc. of America.

Transfer/Customer/user:
New information for scientists on production of Se-enriched crops.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

06 Description:

Presentation "Strategic positioning in obesity prevention research"

Transfer/Customer/user:
Vision of needs and opportunities for impactful research in an academic setting to faculty and students of the Dept of Food Science and Nutrition, Mississippi State University, Starkville, MS.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

07 Description:
Two presentations at the Federation of American Societies for Experimental Biology. The topics were on the dietary Se intake, Se status and methylation status.

Transfer/Customer/user:
New information on Se metabolism and cancer prevention was transferred orally to a group of academic and industrial investigators.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

08 Description:
Three Grand Forks Herald article publications. The topics were healthy foods and cancer prevention.

Transfer/Customer/user:
New information on American food/nutrition choice was transferred to American public.

This major activity has been promoting scientific excellence and an American public view on the scientific nutrition practice. Furthermore, this effort also provides the scientific basis for policy makers.

7. International Cooperation / Collaboration

01 UNITED KINGDOM
We collaborated with the scientists at the University of Surrey, UK, for secondary analyses of mineral balance studies conducted at the Grand Forks Human Nutrition Research Center. These work exchanges take place by email and telephone. We have exchanged data; no funds have been involved.

02 DENMARK
We collaborated with the scientists at the University of Copenhagen, DM, in the speciation of metabolites of selenium. These work exchanges take place by email and telephone. We have exchanged some experimental materials, however, no funds have been involved.

03 UNITED KINGDOM
We collaborated with the scientists at the University of Edinburgh, UK, for studies biomarkers for early detection of cancer. These work exchanges take place by email and telephone. We have exchanged some experimental materials, however, no funds have been involved.

Scientific Publications: Log 115:

Project Number: 5450-51000-045-00D Accession: 0418779 FY: 2013

1. Jackson, M.I., Cao, J.J., Zeng, H., Uthus, E.O., Combs, G.F. 2012. S-Adenosylmethionine-dependent protein methylation Is required for expression of selenoprotein P and gluconeogenic enzymes in HepG2 human hepatocytes. Journal of Biological Chemistry. 287(43):36455-36464. 0000278223

2. Anugu, S., Petersson-Wolfe, C.S., Combs, G.F., Petersson, K.H. 2012. Effect of vitamin E on the immune system of ewes during late pregnancy and lactation. Small Ruminant Research. 111:83-89. 0000283506

3. Moustafa, M., Carlson, B.A., Anver, M.R., Bobe, G., Zhong, N., Ward, J.M., Parella, C.M., Hoffmann, V.J., Rogers, K., Combs, G.F., Schweizer, U., Merlino, G.T., Gladyshev, V.N., Hatfield, D.L. 2013. Selenium and selenoprotein deficiencies induce widespread pyogranuloma formation in mice, while high levels of dietary selenium decrease liver tumor size driven by TGFa . PLoS One. 8(2): e57389. doi:10.1371/journal.pone.0057389. 0000286827

4. Yan, L., Demars, L.C. 2012. Dietary supplementation with methylseleninic acid, but not selenomethionine, reduces spontaneous metastasis of Lewis lung carcinoma in mice. International Journal of Cancer. 131:1260-1266. 0000272038

5. Zeng, H., Liu, J., Jackson, M.I., Zhao, F., Yan, L., Combs, G.F. 2013. Fatty liver accompanies an increase in Lactobacillus species in the hind gut of C57BL/6 mice fed a high-fat diet. Journal of Nutrition. doi:10.3945/jn.112.172460. 0000286572

6. Zeng, H., Cao, J.J., Combs, G.F. 2013. Selenium in bone health: roles in antioxidant protection and cell proliferation. Nutrients. 5:97-110. 0000288824

7. Randhawa, H., Kibble, K., Zeng, H., Mayer, M.P., Reindl, K.M. 2013. Activation of ERK signaling and induction of colon cancer cell death by piperlongumine. Toxicology In Vitro. 27:1626-1633. 0000292878

Approved: MCGUIRE MICHAEL R Date: 09/30/2013

Project Number: 5450-51000-045-02S Accession: 0414720 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: DAVID M KLURFELD Prin Invs: GERALD F COMBS

Start Date: 09/29/2008 Term Date: 05/31/2013

National Programs: 107 N Human Nutrition

Title: FOOD-BASED OBESITY PREVENTION AND HEALTH MAINTENANCE RESEARCH

Period Covered From: 10 / 2012 To: 9 / 2013 Final Report? Yes
Terminate in Two Months? No

Agreement Number: 58-5450-8-0342

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. Objectives (from AD-416):

The objective of this cooperative research is to investigate the role of foods and their components in human health, with particular focus on the prevention of obesity, including the endogenous (biological) and exogenous (psycho-social, environmental) factors that affect the maintenance of healthy body weight and risk to co-morbidities of obesity.

1b. Approach (from AD-416):

Conduct studies with human volunteers to elucidate functions of and quantitative needs for nutrients and/or other components of foods and physical activity in the support of healthy body weight and minimization of risk to chronic disease. Includes focus groups, cross-sectional and clinical intervention studies in both residential and non-residential settings involving volunteers recruited from Grand Forks and other communities.

3. Progress Report:

This report documents research conducted under a Specific Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-045-00D, DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

Twenty-two protocols involving human subjects were managed this year. These were mostly out-patient studies. Twelve were actively collecting data; these addressed seasonality of food and physical activity habits, glycemic effects of honey, glycemic effects of potato, biological assessment of satiety, epigenetic dysregulation in preeclampsia, adoption of standing behavior in use of height-adjustable desks, arranging parks to optimize physical activity and the use of breath 12C:13C ratio to assess energy substrate utilization.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, email communications, discussions at professional conferences/meetings, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-045-04A Accession: 0418389 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: DAVID M KLURFELD Prin Invs: GERALD F COMBS

Start Date: 09/25/2009 Term Date: 09/24/2014

National Programs: 107 N Human Nutrition

Title: HUMAN OBESITY PREVENTION RESEARCH

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 59-5450-9-0336

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. Objectives (from AD-416):

This award will benefit the people of the United States by producing new knowledge that will significantly improve the evidence base for national food, nutrition and health policies. It will bring together two entities, the ARS and the University of North Dakota, each with strong scientific and technical capabilities to produce a combined effort that is unparalleled in its ability to design and conduct human clinical intervention trials addressing the knowledge gaps critical to policy development for reversing the national epidemic of obesity and its co-morbidities. This research will be among the first to test the efficacy and sustainability of U.S. Dietary Guidelines. It will thus be seminal in supporting the further development of those guidelines as well as related national policy concerning food, nutrition and health. Improved national policy will benefit the people of the United States by reducing the prevalence of obesity and obesity-attributable health care costs.

1b. Approach (from AD-416):

This research will address the prevention of childhood/adult obesity, which involves food choices/patterns, physical activity and energy balance, metabolism/physiology, genotype/phenotypic expression, food access/composition, attitudes/traditions, and processes that can lead to diabetes, cancer, heart disease and osteoarthritis. This demands innovative, translational research to generate new knowledge and improve the evidence base for national nutrition/health/food policy. This will be accomplished in this project by addressing the following areas:
1. U.S. Dietary Guidelines Adherence and Healthy Body Weight. Research to identify barriers/ facilitators to adhering to the Dietary Guidelines.
2. Biology of Obesity Prevention. Research on metabolism/physiology affected by diet/physical activity in maintaining healthy body weight; use of "omics" tools to understand individuals' responses to interventions and propensities to gain weight.
3. Food Factors in Maintaining Health & Healthy Body Weight. Research examining the effects of food antioxidants on metabolic responses to exercise.
4. Body Weight and Bone Health. Research on the roles of adiposity and body weight on inflammation and bone health.
5. Diet and Physical Activity in Mitigating Obesity-Promoted Carcinogenesis. Research on the effects of adiposity on the metabolism and anticarcinogenic mechanisms of selenium.

Project Number: 5450-51000-045-04A Accession: 0418389 FY: 2013

3. Progress Report:

This report documents research conducted under a Assistance Type Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-045-00D, DIETARY MODULATION OF OBESITY-RELATED CANCER BY SELENIUM

Please refer to the parent project report for research information.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, email communications, discussions at professional conferences/meetings, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-046-00D Accession: 0419343 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: JAY J CAO

Start Date: 04/09/2010 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: BONE METABOLISM IN OBESITY

Period Covered From: 10 / 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416):

To determine how nutritional, hormonal, and physiological factors affect bone loss/gain in obesity through modifying obesity-induced inflammatory stress. Specifically, we will determine the extent to which obesity is associated with elevated levels of pro-inflammatory cytokines known to promote bone resorption, determine how obesity affects functions of bone cells and bone metabolism, determine the extent to which existing chronic inflammatory stress (induced experimentally by lipopolysaccharide implantation), estrogen deficiency (affected by ovariectomy), and subclinical magnesium intake impair bone health in obese animal models and in obese human subjects, and determine how moderate physical activity preserves bone structure as compared to caloric restriction during weight reduction in an obese animal model.

1b. Approach (from AD-416):

Studies will utilize cell culture, animal models and human subjects. We will use diet-induced obese mice or rats to determine the mechanisms by which adiposity interacts with other dietary, hormonal and physiological factors, such as estrogen deficiency, chronic inflammation, magnesium intake, and moderate exercise, and affects bone structure and functions of osteoblasts and osteoclasts. Human studies will use the in-house Community Studies Unit and the Metabolic Research Unit to conduct supplementation and controlled feeding experiments, respectively. We will determine whether 300 mg/d Mg supplementation to obese postmenopausal women with suspected marginal magnesium deficiency, ameliorates pro-inflammatory cytokine production and improves biomarkers of bone resorption and formation balance.

2. Milestones for FY2013:

1. Complete laboratory and statistical analyses of Mg supplementation of obese postmenopausal women study; report findings from the study
   Milestone Not Met
   Critical vacany (quantitative or qualitative deficiency in personnel
   The SY has retired and the vacancy has not been filled.
2. Report animal study on exercise on bone metabolism
   Milestone Substantially Met

3. Progress Report:

A human study was completed to determine optimal protein intake and musculoskeletal response to energy deficit. Thirty-nine physically active volunteers aged 18 - 42 were recruited to participate in a 31-d live-in, controlled feeding study. Subjects were

randomly assigned to three dietary groups: high protein (2.4 g/kg/d), moderate protein (1.6 g/kg/d), or low protein (0.8 g/kg/d). Markers of bone turnover were assessed. Calcium absorption was determined using stable isotope methodology. Muscle biopsies, and various molecular techniques, direct measures of muscle protein synthesis, protein breakdown, and the cellular mechanisms that regulate these processes were also assessed following energy sufficient and insufficient diets. Samples have been analyzed and data have been summarized and submitted for publication.

A study was conducted with cells and animals to determine whether supplementation of N-acetylcysteine, an antioxidant, affects osteoclast formation and mitigates deterioration of bone microstructure in mice fed a high-fat diet. Forty-eight 6-wk-old male C57BL/6 mice were randomly assigned to four treatment groups (n=12/group) and fed either a normal-fat (10% energy as fat) or a high-fat (45% energy as fat) diet ad libitum with or without N-acetylcysteine supplementation (1 g/kg diet) for 17 wks. Changes in osteoclast number in vitro, bone structure, and other serum markers related to bone metabolism were measured.

4. Accomplishments

01 Short-term weight loss by diet and exercise while eating a high-protein diet does not compromise bone health. ARS scientists at Grand Forks, ND, in collaboration with US Army scientists conducted a 31-d live-in, controlled feeding study to determine whether bone metabolism is affected by a high protein diet during weight loss. Data demonstrated that consuming dietary protein at levels above the RDA did not significantly alter bone metabolism. These results will enhance the understanding of the role of high-protein intake in the maintenance of bone heath. The findings can be used by the Dietary Guidelines for Americans (DGA) as the evidence in supporting the use of high-protein diets during periods of weight loss to prevent muscle loss without harming bone metabolism.

107	2	A	2009
107	3	A	2009

5. Significant Activities that Support Special Target Populations:

None

6. Technology Transfer:

0	Number of New CRADAs
0	Number of Active CRADAs
0	Number of New MTAs (providing only)
0	Number of Invention Disclosures Submitted
0	Number of Patent Applications Filed
0	Number of New Germplasm Releases
0	Number of new commercial licenses granted
0	Number of web sites managed
0	Number of non-peer reviewed presentations and proceedings
0	Number of newspaper articles and other presentations for non-science audiences
1	Number of Other Technology

Other Technology Details:

01 Description:

Project Number: 5450-51000-046-00D Accession: 0419343 FY: 2013

Calcium homeostasis and bone metabolic responses to high protein, energy deficit diets in healthy young adults: a randomized control trial. Experimental Biology 2013, Boston, April 22, 2013.

Transfer: Information about how dietary protein affects Ca absorption and bone health in humans

Customer/user: Scientists and nutritionists

Impact/outcome: Information on the impact of protein intake on bone metabolism can be used as a dietary guideline to promote bone health.

7. International Cooperation / Collaboration

Scientific Publications: Log 115:

1. Nielsen, F.H. 2012. Calcium, magnesium, and potassium in food. In: Sulewski, G., editor. Fertilizing Crops to Improve Human Health: A Scientific Review. 1st edition. Norcross, GA: International Plant Nutrition Institute, p. 123-142. 0000264517

2. Zhu, L., Cao, J.J., Sun, M., Yuen, T., Zhou, R., Li, J., Peng, Y., Moonga, S.S., Guo, L., Mechanick, J.I., Iqbal, J., Peng, L., Blair, H.C., Biam, Z., Zaidi, M. 2012. Vitamin C reverses hypogonadal bone loss. PLoS One. 7(10):1-6. 0000280483

3. Nielsen, F.H. 2012. History of zinc in agriculture. Advances in Nutrition. 3:783-789. 0000289773

4. Baliram, R., Sun, L., Cao, J.J., Li, J., Latif, R., Huber, A.K., Yuen, T., Blair, H.C., Zaidi, M., Davies, T.F. 2012. Hyperthyroid-associated osteoporosis is exacerbated by the loss of TSH signaling. Journal of Clinical Investigation. 122(10):3737-3741. 0000291631

5. Shen, C., Cao, J.J., Dagda, R., Chanjaplammootil, S., Lu, C., Chyu, M., Gao, W., Wang, J., Yeh, J.K. 2012. Green tea polyphenols benefits body composition and improves bone quality in long-term high-fat diet-induced obese rats. Nutrition Research. 32:448-457. 0000269765

6. Yan, C., Wu, M., Cao, J.J., Tang, H., Zhu, M., Johnson, P.E., Gao, H. 2012. Critical role for CCAAT/Enhancer-binding protein beta in immune complex-induced acute lung injury. Journal of Immunology. 189(3):1480-90. 0000280484

7. Zhu, L., Blair, H.C., Cao, J.J., Yuen, T., Latif, R., Guo, L., Tourkova, I.L., Li, J., Davies, T.F., Sun, L., Bian, Z., Rosen, C., Zallone, A., New, M.I., Zaidi, M. 2012. Blocking antibody to the beta-subunit of FSH prevents bone loss by inhibiting bone resorption and stimulating bone synthesis. Proceedings of the National Academy of Sciences. 109(36):14574-14579. 0000285708

8. Colaianni, G., Sun, L., Di Benedetto, A., Tamma, R., Zhu, L., Cao, J.J., Grano, M., Yuan, T., Colucci, S., Cuscito, C., Mancini, L., Li, J., Nishimori, K., Bab, I., Lee, H., Iqbal, J., Young, W., Rosen, C., Zallone, A., Zaidi, M. 2012. Bone marrow oxytocin mediates the anabolic action of estrogen on the skeleton. Proceedings of the National Academy of Sciences. 287(34):29159-29167. 0000280488

Project Number: 5450-51000-046-00D Accession: 0419343 FY: 2013

9. Pasiakos, S.M., Cao, J.J., Margolis, L.M., Sauter, E.R., Whigham Grendell, L.D., Mcclung, J.P., Rood, J.C., Carbone, J.W., Combs, G.F., Young, A.J. 2013. Effects of high protein diets on fat-free mass and muscle protein synthesis following weight loss: a randomized controlled trial. Journal of Federation of American Societies for Experimental Biology. doi: 10.1096/fj.13-230227. 0000287668

Approved: MCGUIRE MICHAEL R Date: 09/30/2013

Project Number: 5450-51000-048-00D Accession: 0419645 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: MATTHEW J PICKLO

Start Date: 05/27/2010 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH

Period Covered From: 10/ 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Progress and Outcomes:

1a. Objectives (from AD-416):

1. Determine the extent to which dietary antioxidants alter obesity-induced and/or exercise-induced changes in mitochondrial function and insulin sensitivity.
Sub-objective 1A. Determine the influence of anti-oxidant supplementation on changes in insulin sensitivity induced in the rat by high dietary fat and exercise.
Sub-objective 1B. Determine the degree to which anti-oxidant supplementation alters exercise-induced changes in insulin sensitivity and mitochondrial function responses of overweight/obese individuals.
2. Identify sites and causes of obesity-induced and exercise-induced oxidative stress.
Sub-objective 2A. Determine the effects of obesity and exercise on the temporal and cellular activation of the nuclear factor (erythroid-derived 2)-like 2 (Nrf-2)/Anti-oxidant Response Element pathway.
Sub-objective 2B. Identify and characterize obesity-induced and exercise-induced oxidative changes to insulin signaling pathway proteins.
3. Identify, characterize and compare sites of obesity-induced versus exercise-induced mitochondrial respiratory changes.
Sub-objective 3A. Determine the degree to which anti-oxidant supplementation blunts exercised-induced and obesity-induced changes in mitochondria.

1b. Approach (from AD-416):

In order to complete the objectives of this proposal, we will utilize a combination of studies in humans, rodents that examine physiologic, metabolomic, genetic, and proteomic endpoints. In Objective 1, we will perform studies in humans and rodents to determine how antioxidant (vitamin E and vitamin C) supplementation affects insulin responses to exercise and obesity. The study in humans will involve analysis of exercise adaptation and insulin responses in previously untrained individuals and if antioxidant supplementation either enhances or negates these adaptations. Rodent studies will further examine molecular mechanisms underlying these adaptations.
In Objective 2, we will determine the extent to which obesity, exercise, and anti-oxidant supplementation alter redox balance in animals and specific cells and to identify specific proteins whose thiol redox status is altered in obesity, exercise, and anti-oxidant supplementation. These studies will utilize transgenic mouse models and proteomic approaches.
In Objective 3, we will determine the extent to which obesity, exercise, and anti-oxidant supplementation alter mitochondrial function. These studies will utilize rat models of exercise and obesity. Whole tissue and isolated mitochondria will be studied for changes in total mitochondrial content, mitochondrial gene expression, and respiration, and mitochondrial enzyme activities.

Project Number: 5450-51000-048-00D Accession: 0419645 FY: 2013

2. Milestones for FY2013:

1. We will perform initial experiments to determine exercise parameters, perform anti-oxidant supplementation studies in obese and exercising rats, and perform glucose, insulin, fatty acid analyses.
   Milestone Fully Met

2. We will perform analyses for redox status and insulin signaling proteins and write/submit manuscripts for publication.
   Milestone Substantially Met

3. We will perform studies on 18 subjects and process samples.
   Milestone Not Met
   No longer applies (Milestone no longer necessary)
   Milestone no longer applicable.
4. We will perform experiments on obese and exercising ARE/hPAP mice w/ anti-oxidant supplementation, determine the activity and localization of ARE/hPAP transgene in these conditions, analyze data, and write/submit manuscripts for publication.
   Milestone Not Met
   No longer applies (Milestone no longer necessary)
   Milestone no longer applicable.
5. We will develop methods for analysis of PTEN and PTP1B from rat samples from sub-objective 1A.
   Milestone Not Met
   Insufficient resources (lack of operational funds)
   Lack of operational funds.
6. We will perform the animal studies examining mitochondrial effects of obesity and exercise with anti-oxidant supplementation. We will perform analyses on mitochondrial samples, analyze data, and write/submit publications.
   Milestone Substantially Met

3. Progress Report:

Objective 1A. During FY 2013 we completed two studies testing the hypotheses that supplementation with the antioxidants alpha-tocopherol and vitamin C exacerbated insulin resistance under (1) sedentary and (2) exercising conditions.

For experiment 1, obese-prone rats were fed a eucaloric diet (10% fat energy), or a hypercaloric (45% fat energy) diet for 12 weeks, or a hypercaloric diet supplemented with d-alpha-tocopherol acetate and vitamin C. Our data demonstrated that the hypercaloric diet induced glucose intolerance and that extent of glucose intolerance was not modified by supplementation with the anti-oxidants. Data also indicated that supplementation did not alter levels of adipose inflammation and macrophage infiltration. These data indicate that antioxidant supplementation does not modify obesity-induced hyperglycemia. This work is being prepared for publication.

For experiment 2, obese-prone rats were made obese by feeding a hypercaloric diet for 12 weeks. Obese animals were then exercised for a further 12 weeks with and without supplementation with d-alpha-tocopherol acetate and vitamin C. Our data demonstrated that glucose tolerance, once established, was not ameliorated by the 12 week exercise regimen even though the body composition of the exercise rats returned to that of the control, eucaloric-fed rats. Anti-oxidant supplementation did not modify the glucose response to exercise. These data indicate that exercise alone is not able to reduce pre-existing hyperglycemia and that antioxidant supplementation has no positive or negative effects. Samples from this study are currently being processed.

Project Number: 5450-51000-048-00D Accession: 0419645 FY: 2013

Objective 2B. Previously, we demonstrated that obesity reduces protein modification by glutathione, a process termed glutathionylation, in visceral adipose tissue obtained from obese rats. In order to fully explore this finding, we developed more quantitative ways of measuring glutathionylation using liquid chromatography coupled to mass spectrometry. We are currently preparing these results for publication.

4. Accomplishments

01 Antioxidants and high-blood sugar. Obesity-induced hyperglycemia (high blood sugar) is a problem facing over 75 million Americans. Although many Americans take antioxidant supplements, some reports suggest that antioxidant supplements may make hyperglycemia worse. ARS scientists at Grand Forks, ND, determined that supplementation with the antioxidants vitamin E and vitamin C did not worsen or prevent hyperglycemia in rats fed a high-calorie, high fat diet. These results suggest that supplementation with vitamin C and vitamin E has no effect on the development of high blood sugar.

107 2 A 2009

5. Significant Activities that Support Special Target Populations:

None

6. Technology Transfer:

0 Number of New CRADAs
0 Number of Active CRADAs
0 Number of New MTAs (providing only)
0 Number of Invention Disclosures Submitted
0 Number of Patent Applications Filed
0 Number of New Germplasm Releases
0 Number of new commercial licenses granted
0 Number of web sites managed
0 Number of non-peer reviewed presentations and proceedings
0 Number of newspaper articles and other presentations for non-science audiences
6 Number of Other Technology

Other Technology Details:

01 Description:
Newspaper article

Picklo MJ. "Go Fish" Grand Forks Herald, Grand Forks, ND. July 2013. Customer/user: General lay population of Grand Forks, ND area Impact/outcome: Inform and educate general public about the health benefits of eating fish.

02 Description:
Presentation for International society meeting

Picklo M, Raatz S, Cleveland B, Rexroad C III. Evaluation of long-chain n3 fatty acid content in diploid and triploid rainbow trout. American Society for Nutrition/Experimental Biology, Boston, MA 2013.Customer/user: Scientists, health professionals, nutritionists. Impact/outcome: Demonstrated that the Nrf2 transcription factor regulates exercise capacity in male but not female mice. Indicates that

anti-oxidant pathways also affect energy metabolism pathways.

03 Description:

Presentation for International society meeting

Picklo M. Vitamin E and Vitamin C supplementation does not prevent glucose intolerance in obese-prone rats. American Society for Nutrition/Experimental Biology, Boston, MA 2013.Customer/user: Scientists, health professionals, nutritionists.
Impact/outcome: Demonstrated that specific anti-oxidant enzyme pathways are reduced during adipocyte hypertrophy.

04 Description:

Taught two lectures on Spectroscopy and Chromatography, University of North Dakota, January, 2013
Customer/user: Graduate Students
Impact/outcome: Taught graduate level science students principles of light spectroscopy and chromatography.

05 Description:

Planned and directed GFHNRC booth at 2013 Health Care Expo, Grand Forks North Dakota. Organized talks and demonstrations by Center scientists. Over 2000 attendees
Customer/user: General lay population of Grand Forks, ND area
Impact/outcome: Promoted healthy nutrition guidelines for community; enhanced visibility of the GFHNRC, assisted with recruiting volunteers for nutrition studies.

06 Description:

Invited Presentation "Developing the Relationship of ARS Aquaculture and Nutrition: Fish Consumption and Omega-3's". USDA/ARS National Center for Cold and Cool Water Aquaculture, Kearneysville, WV, July 2012.
Customer/user: ARS scientists
Impact/outcome: Promote intra-programmatic collaboration between the ARS National Programs in Aquaculture and Nutrition.

7. International Cooperation / Collaboration

Scientific Publications: Log 115:

1. Raatz, S.K., Rosenberger, T.A., Johnson, L., Wolters, W.R., Burr, G.S., Picklo, M.J. 2013. Dose-dependent consumption of farmed Atlantic salmon (salmo salar) increases plasma phospholipid n-3 fatty acids differentially. Journal of the Academy of Nutrition and Dietetics. 113(2):282-287. 0000280760

2. Raatz, S.K., Silverstein, J., Jahns, L.A., Picklo, M.J. 2013. Issues of fish consumption for cardiovascular disease risk reduction. Nutrients. 5:1081-1097. 0000290071

3. Picklo, M.J., Idso, J.P., Jackson, M.I. 2013. S-Glutathionylation of hepatic and visceral adipose proteins decreases in obese rats. Obesity. 21:297-305. 0000276812

4. Gonnella, T.P., Keating, J.M., Kjemhus, J.A., Picklo, M.J., Biggane, J.P. 2013. Fluorescence lifetime analysis and effect of magnesium ions on binding of NADH to human aldehyde dehydrogenase 1. Chemico Biological Interactions. 0000285320

Project Number: 5450-51000-048-00D Accession: 0419645 FY: 2013

202(1-3):85-90.

5. Raiten, D.J., Namaste, S., Brabin, B., Combs, G.F., L'Abbe, M.R., Wasantwisut, E., Darnton-Hill, I. 2011. Executive summary: biomarkers of nutrition for development: building a consensus. American Journal of Clinical Nutrition. 94(2):6335-650S. 0000268236

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-048-01N Accession: 0420147 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: MARY J KRETSCH Prin Invs: GERALD F COMBS

Start Date: 09/01/2010 Term Date: 08/31/2015

National Programs: 107 N Human Nutrition

Title: HEALTHY BODY WEIGHT RESEARCH

Period Covered From: 10/2012 To: 9 /2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-0-0111N

Organization Name: US ARMY RES INST ENVIR MEDICINE

Progress and Outcomes:

1a. Objectives (from AD-416):

Collaborate in planning, implementation and reporting of research on the effects of diet and physical activity in maintaining healthy body weight.

1b. Approach (from AD-416):

Human volunteers will be studied under a variety of diety conditions and physical activity regimens, and biochemical and functional parameters will be measured.

3. Progress Report:

This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the US ARMY RES INST ENVIR MEDICINE. Additional details for the research can be found in the report for the parent project 5450-51000-048-00D, FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH

Studies were conducted to determine the effect of dietary protein level of the status of muscle protein and bone mineral during a 30-day period of negative energy balance. This was done in young men and women volunteers who lived in our metabolic unit and were subjected to a 30% energy deficit by dietary means with a 10% increase in energy output by prescribed physical activity. Bone mineral was evaluated by the retention of an infuse dose of stable calcium; protein accretion was determined by the uptake of an infused dose of stable isotopically labeled amino acids into samples of thigh muscle collected by biopsy. The active experimental phase of this study was completed in FY2012; samples are being analyzed. Results show that moderately increased protein intake can reduce the loss of muscle protein that occurs under conditions of negative caloric balance in exercising men and women.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, site visits, email communications, discussions at professional conferences/meetings, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-048-02S Accession: 0420151 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: GERALD F COMBS

Start Date: 09/01/2010 Term Date: 08/31/2015

National Programs: 107 N Human Nutrition

Title: CLINICAL RESEARCH

Period Covered From: 10/ 2012 To: 9 / 2013 Final Report? No
Terminate in Two Months? No

Agreement Number: 58-5450-0-0342

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. Objectives (from AD-416):

This project will benefit the people of the United States by facilitating the production of new knowledge that will significantly improve the evidence base for national food, nutrition and health policies. It will bring together two entities, the USDA-ARS and the University of North Dakota, as represented by the School of Medicine and Health Sciences (UND-SMHS), each with strong scientific and technical capabilities, to produce a combined effort that is unique in its ability to design and conduct human clinical intervention trials addressing the knowledge gaps critical to reversing the national epidemic of obesity and its co-morbidities. This partnering advances the mission of the Grand Forks Human Nutrition Research Center (GFHNRC) in regard to its conducting research with human subjects.

1b. Approach (from AD-416):

Partnering with the UND-SMHS will enhance the research mission of the USDA-ARS GFHNRC in the areas of clinical research in human nutrition, metabolism, and physiology. The UND-SMHS will bring necessary expertise in medicine and human health surveillance. Health oversight by UND-SMHS licensed physicians will be a valuable contribution provided for conducting human nutrition research. The combined effort will produce synergy resulting in a unique capability for conducting human clinical trials addressing the prevention of obesity. Those trials will address the following areas:
1. Sustainability of diet/physical activity practices consistent with the Dietary Guidelines for Americans.
2. Roles of diet and physical activity in mitigating obesity-related diseases, diabetes, cancer and bone loss.
These clinical trials will be among the first designed to test the Dietary Guidelines for Americans in a healthy population. This research will support further enhancement of the dietary guidelines as well as related national policies concerning food, nutrition and health.

3. Progress Report:
This report documents research conducted under a Specific Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-048-00D, FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH

This project provided clinical research support for eight human studies protocols in

Project Number: 5450-51000-048-02S Accession: 0420151 FY: 2013

FY2013. These included a study of the effect of dietary protein on muscle protein and bone mineral retention during negative energy balance in which this project provided the expertise for performing muscle biopsies. This project also provided the health surveillance oversight for 21 other active human protocols that addressed seasonality of food and physical activity habits, glycemic effects of honey, glycemic effects of potato, biological assessment of satiety, epigenetic dysregulation in preeclampsia, adoption of standing behavior in use of height-adjustable desks, arranging parks to optimize physical activity and the use of breath 12C:13C ratio to assess energy substrate utilization.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, email communications, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

FINAL PROGRESS REPORTS

OF

TERMINATED CRIS WORK UNITS

Project Number: 5450-51000-047-01G Accession: 0422778 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: DAVID M KLURFELD Prin Invs: KATE J CLAYCOMBE

Start Date: 04/01/2012 Term Date: 03/31/2013

National Programs: 107 N Human Nutrition

Title: EXPERIMENTAL BIOLOGY 2012 SYMPOSIUM: ADIPOSE DYSFUNCTION INTERACTION OF ROS AND INFLAMMATION

Period Covered From: 10/ 2012 To: 9 / 2013 Final Report? Yes
Terminate in Two Months? Yes

Agreement Number: 59-5450-2-0302

Organization Name: AMERICAN SOC FOR NUTRITION

Progress and Outcomes:

1a. Objectives (from AD-416):

The major purpose of this symposium is to enhance the visibility of the importance of research conducted at ARS by 1) fostering ARS objectives of providing a forum for the cutting edge reasearch presented by prominent scientists and to have symposium participants meet, network and exchange ideas with other leading investigators in their field, and 2) by showcasing the USDA Agricultural Research Service (ARS) strategic goal "No. 5.2.2: Define the role of nutrients, foods, and dietary patterns in growth, maintenance of health, and prevention of obesity and other chronic diseases".

The goal of this symposium is to provide a forum for the discussion of how oxidant signaling is altered in adipose tissue as a result of obesity. Recent data indicate that adipose dysfunction in obesity involves interactions between inflammatory pathways and reactive oxygen signaling. While numerous studies indicate that oxidant stress is elevated overall in the body as a result of obesity, there is now only a growing literature detailing the role of oxidant stress and oxidant stress signaling pathways in the regulation and dysfunction of adipose tissue itself. However, there is an incomplete understanding of the relationships of the cell types comprising adipose, their interplay in obesity, and the role oxidant stress that influences these relationships. Furthermore, the inflammatory processes present in obese adipose tissue modulates cellular oxidant stress and responses to oxidant stress. The speakers chosen to present data and to discuss this topic are highly-regarded and have made seminal contributions to the understanding of this area.

1b. Approach (from AD-416):

Two ARS scientists and one cooperator will serve as organizing co-chairs of this symposium. Four invited speakers, who will each present 30 minute oral talks, are highly-regarded and have made seminal contributions to the understanding of this area.

3. Progress Report:
This report documents research conducted under a Grant between ARS and the AMERICAN SOC FOR NUTRITION. Additional details for the research can be found in the report for the parent project 5450-51000-047-00D, BIOLOGY OF OBESITY PREVENTION

This ASN symposium entitled "Adipose Dysfunction: Interaction of ROS and Inflammation"

Project Number: 5450-51000-047-01G Accession: 0422778 FY: 2013

was organized and held at the Experimental Biology 2012 meeting, April 24, 2012, in San Diego, CA. This symposium was partially funded by USDA ARS Professional Activities Grant to an ARS scientist. From the four invited speaker presentations, attendees of this symposium gained a greater understanding of the interactions that inflammatory stimuli and reactive oxygen species (ROS) have upon adipose tissue function and dysfunction. In conclusion, it was also clear that adipose dysfunction is a complex phenomenon, which includes the interplay of multiple cell types and several signaling pathways. Symposium summary was published in Advances in Nutrition Journal in 2012.

Publication:
Picklo M, Claycombe KJ, Meydani M: Adipose dysfunction, interaction of reactive oxygen species, and inflammation. Adv Nutr 2012, 3(5):734-735.

ARS PI monitoring activities to evaluate research progress included: email communications, discussions at professional conferences/meetings.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-047-02N Accession: 0422898 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: DAVID M KLURFELD Prin Invs: KATE J CLAYCOMBE

Start Date: 01/01/2013 Term Date: 09/30/2014

National Programs: 107 N Human Nutrition

Title: EPIGENOMIC DYSREGULATION IN PREECLAMPSIA-ASSOCIATED CHRONIC HYPERTENSION

Period Covered From: 10 / 2012 To: 9 / 2013 Final Report? Yes
Terminate in Two Months? Yes

Agreement Number: 58-5450-3-0003N

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. Objectives (from AD-416):

The objective of this research is to identify distinct epigenetic patterns of DNA methylation associated with preeclampsia that underlie the future development of hypertension and to determine the implication on responses to moderators and therapeutic interventions in the management of chronic hypertension. Univariate analysis of variance will be used to test associations between DNA methylation in genes and chronic hypertension among women with and without a history of preeclampsia. We will use multiple linear regression to examine differences in treatment responses to high blood pressure based on DNA methylation patterns, dietary intake, activity and BMI in candidate cardiovascular genes.

1b. Approach (from AD-416):

Women diagnosed with chronic hypertension, aged 30-50 years (limiting the likelihood of morbid conditions), with (group 1, n=20) and without (group 2, n=20) a history of preeclampsia will be recruited. A medical history including smoking, pregnancy, preeclampsia, hypertension; non-pharmacologic and pharmacologic treatment strategies; dietary intake (Dietary History Questionnaire II), activity patterns, BMI, laboratory values relative to cardiovascular disease will be collected. The EndoPat (Itamar) will be used to non-invasively measure endothelial function. Venipuncture will be used to obtain blood samples for DNA analysis (DNA methylation) and laboratory measures of cardiovascular risk (inflammation).

3. Progress Report:
This report documents research conducted under a Non Funded Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-047-00D, BIOLOGY OF OBESITY PREVENTION

This study was terminated effective June 28th 2013 due to departure of the principal non-USDA affiliate investigator from the University of North Dakota. A total of 12 participants who were recruited, data were collected for endothelial function measurements, diet history information, body composition, and blood pressures. Due to premature termination of this project, no overall study conclusion can be drawn from the data.

ARS PI monitoring activities to evaluate research progress included: email communications.

Project Number: 5450-51000-047-02N Accession: 0422898 FY: 2013

Approved: MCGUIRE MICHAEL R Date: 08/21/2013

Project Number: 5450-51000-048-04S Accession: 0421840 FY: 2013

ModeCode: 5450-20-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
DIETARY PREVENTION OF OBESITY-RELATED DISEASE RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: MATTHEW J PICKLO

Start Date: 08/01/2011 Term Date: 07/31/2013

National Programs: 107 N Human Nutrition

Title: EVALUATE THE NUTRITIONAL ADEQUACY AND EFFECTS OF DIETARY FATS AND LIPIDS

Period Covered From: 10/2012 To: 9 /2013 Final Report? Yes
Terminate in Two Months? No

Agreement Number: 58-5450-1-0345

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. Objectives (from AD-416):

To determine how salmon consumption alters lipid oxidation parameters in human plasma. In this work, we will quantify the content of omega-6 and omega-3 fatty acids in the plasma from participants in the GFHNRC human study that have consumed differing amounts of salmon as a source of omega-3 fatty acids. These data will provide information on the role of fish consumption upon markers of inflammation and oxidative stress. Attainment of this data may be useful in future deliberations of the dietary guidelines committee on the evidence base for long chain omega-3 fatty acid recommended intake levels.

1b. Approach (from AD-416):

The GFHNRC will perform the necessary salmon feeding trial and collection of plasma samples. Samples of plasma will be delivered to the cooperator for analysis of fatty acid oxidation products. The cooperator will also offer expertise in interpretation and writing of the results. Data will be presented and published with GFHNRC scientists and the cooperator as authors. The cooperator will also offer expertise in interpretation of the results of the phospholipid fatty acids.

3. Progress Report:

This report documents research conducted under a Specific Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-048-00D, FOOD FACTORS AND MAINTENANCE OF BODY WEIGHT AND HEALTH

The GFHNRC completed the necessary salmon feeding trial in people and collection of plasma samples. The cooperator analyzed the plasma for content of fatty acids in the plasma phospholipids. The cooperator offered expertise in interpretation and writing of the results. Data were presented at the Experimental Biology meeting April 2012. The results were published with GFHNRC scientists and the cooperator as authors.

Raatz SK, Rosenberger TA, Johnson LK, Wolters WW, Burr GS, Picklo MJ. Dose-dependent consumption of farmed Atlantic salmon (Salmo salar) increases plasma phospholipid n-3 fatty acids differentially. Journal of the Academy of Nutrition and Dietetics. 2013 Feb;113(2):282-7.

This work also led to an ancillary paper:

Project Number: 5450-51000-048-04S **Accession:** 0421840 **FY:** 2013

Raatz SK, Golovko MY, Brose SA, Rosenberger TA, Burr GS, Wolters WR, Picklo MJ. Baking Reduces Prostaglandin, Resolvin, and Hydroxy-Fatty Acid Content of Farm- Raised Atlantic Salmon (Salmo salar). Journal of Agricultural and Food Chemistry. 2011 Oct 26;59(20):11278-8644.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, on-site Cooperator/ARS meetings, email communications.

Approved: MCGUIRE MICHAEL R **Date:** 08/21/2013

Project Number: 5450-51000-049-09S Accession: 0421842 FY: 2013

ModeCode: 5450-10-00 NORTHERN PLAINS AREA
GRAND FORKS HUMAN NUTRITION RESEARCH CENTER (GRAND FORKS, ND)
HEALTHY BODY WEIGHT RESEARCH

NPL Leader: JOHN W FINLEY Prin Invs: SUSAN K RAATZ

Start Date: 08/01/2011 Term Date: 05/31/2013

National Programs: 107 N Human Nutrition

Title: EVALUATE THE NUTRITIONAL ADEQUACY AND EFFECTS OF DIETARY FATS AND LIPIDS

Period Covered From: 10/ 2012 To: 9 / 2013 Final Report? Yes
Terminate in Two Months? No

Agreement Number: 58-5450-1-0341

Organization Name: UNIVERSITY OF NORTH DAKOTA

Progress and Outcomes:

1a. Objectives (from AD-416):

To determine how salmon consumption alters lipid oxidation parameters in human plasma. In this work, we will quantify the content of omega-6 and omega-3 fatty acids in the plasma from participants in the GFHNRC human study that have consumed differing amounts of salmon as a source of omega-3 fatty acids. These data will provide information on the role of fish consumption upon markers of inflammation and oxidative stress. Attainment of this data may be useful in future deliberations of the dietary guidelines committee on the evidence base for long chain omega-3 fatty acid recommended intake levels.

1b. Approach (from AD-416):

The GFHNRC is responsible for performance of studies to assess the role of nutrition in obesity prevention and in the reduction of obesity related chronic diseases. The GFHNRC will perform the necessary salmon feeding trial and collection of plasma samples. Samples of plasma will be delivered to the cooperator for analysis of fatty acid oxidation products. The cooperator will also offer expertise in interpretation and writing of the results. Data will be presented and published with GFHNRC scientists and the cooperator as authors. The cooperator will also offer expertise in interpretation of the results of the phospholipid fatty acids.

3. Progress Report:

This report documents research conducted under a Specific Cooperative Agreement between ARS and the UNIVERSITY OF NORTH DAKOTA. Additional details for the research can be found in the report for the parent project 5450-51000-049-00D, DIETARY GUIDELINES ADHERENCE AND HEALTHY BODY WEIGHT MAINTENANCE

All work on this project has been completed.

ARS PI monitoring activities to evaluate research progress included: phone calls/conference calls, email communications, review of Accomplishment Report.

Approved: MCGUIRE MICHAEL R Date: 08/21/2013